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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/508,781

09/19/2005

Tai-Tung Yip

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EXAMINER

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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/508,781	<b>Applicant(s)</b> YIP ET AL.	
	<b>Examiner</b> Nina A. Archie	<b>Art Unit</b> 1645	

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 23 May 2008.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-14 is/are pending in the application.
- 4a) Of the above claim(s) 8-14 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-7 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                     | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____                                      |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)          | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____  | 6) <input type="checkbox"/> Other: _____                          |

### **DETAILED ACTION**

1. This Office Action is responsive to Applicant's amendment and response filed on 5/23/2008 has been entered into the record. Claims 1-14 are pending. Claims 1, 8, 14 have been amended.

#### **Objections Withdrawn**

2. In view of the Applicant's amendment and remark following objections/rejections are withdrawn.

a) Objection to specification is withdrawn in light of applicant's amendment thereto.

#### ***Claim Rejections Maintained***

##### ***35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

3. Claims 1-7 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention are maintained for the reasons set forth in the previous office action. This is a written description rejection.

#### **Applicant arguments:**

Proceeding under his faulty restriction requirement, the examiner focuses on a single protein marker, I-M38. The examiner simply asserts that the specification lacks written description because "It]he specification does not teach any structural limitations of I-M38." Office Action, pg. 5, ¶ 2. The examiner's assertion is legally flawed, however.

Contrary to the examiner's assertion, § 112 does not require the specification to provide the structure of I-M38. All that is required to satisfy the "written description" requirement of § 112, according to the Federal Circuit, is that the application convey with reasonable clarity to those skilled in the art that, as of the filing date sought, applicant was in possession of the claimed invention. See *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 1563 (Fed. Cir. 1991).

In the instant case, the claims are directed to methods of qualifying hepatocellular carcinoma status in a subject, comprising analyzing a biological sample from the subject for a diagnostic level of one or more specific protein markers. The specification explains how to analyze a biological sample for each of the noted biomarkers. See, e.g. Application, pg. 10-14, Examples 1-3, and Figures 1 & 2. For instance, a serum sample is analyzed for a level of protein marker I-M38 by exposing serum fraction 6 to an IMAC3 ProteinChip® Array and determining the concentration of a protein with a molecular weight of approximately 8,942 daltons. *Id.* Furthermore, Examples 1-3 show that applicants used the claimed biomarkers, including I-M38, to evaluate 40 patients with hepatocellular carcinoma (HCC) and 21 patients with chronic liver disease (CLD). Using the claimed biomarkers, applicants distinguished HCC patients from CLD patients with a high degree of success, i.e., greater than 85%. For example, see application at pages 15-19.

Accordingly, one of skill in the art would readily recognize that, as of the filing date, applicants were in possession of the claimed methods. The rejection, therefore, should be withdrawn.

**Examiner's Response to Applicant's Arguments:**

Examiner accepts applicant's amendments. However applicant's argument is not deemed persuasive. Although the written description requirement does not require a complete structure, examples of what can satisfy the requirement of written description are: structure, formula, chemical name, or physical properties, all of which are lacking in the instant application.

*The Regents of the University of California v. Eli Lilly* (43 USPQ2d 1398-1412), the court held that a generic statement which defines a genus by only their functional activity does not provide an adequate written description of the genus. The court indicated that while Applicants are not required to disclose every species encompassed by a genus, the description of a genus is achieved by the recitation of a representative number of DNA molecules, usually defined by a nucleotide sequence, falling within the scope of the claimed genus. At section B(1), the court states that "An adequate written description of a DNA... requires a precise definition, such as by structure, formula, chemical name, or physical properties, not a mere wish or plan for obtaining the claimed chemical invention."

As outlined previously, the instant claims are to drawn to a method for qualifying hepatocellular carcinoma in a subject comprised of analyzing a biological sample from said subject for a diagnostic level of a protein. The specification discloses that Figures 1-2 disclose a molecular weight of I-M38. The specification does not teach any structural limitations of I-M38. Therefore, the specification lacks written description of the claimed method for qualifying hepatocellular carcinoma in a subject comprised of analyzing a biological sample from said subject for a diagnostic level of a protein. This issue is best resolved by Applicants pointing to the specification by page and line number where description of the claimed invention is set forth.

MPEP § 2163.02 states, "an objective standard for determining compliance with the written description requirement is, 'does the description clearly allow persons of ordinary skill in the art to recognize that he or she invented what is claimed'. The courts have decided: The purpose of the "written description" requirement is broader than to merely explain how to "make and use"; the applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the "written description" inquiry, whatever is now claimed. See *Vas-Cath, Inc.'v. Mahurkar*, 935 F.2d 1555, 1563-64, 19 USPQ2d 1111, 1117 (Federal Circuit, 1991 ). Furthermore, the written description provision of 35 USC § 112 is severable from its enablement provision; and

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adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (CAFC 1993) and *Amgen Inc. V. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

The Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, paragraph 1, "'Written Description' Requirement (66 FR 1099-1111, January 5, 2001) state, "[p]ossession may be shown in a variety of ways including description of an actual reduction to practice, or by showing the invention was 'ready for patenting' such as by disclosure of drawings or structural chemical formulas that show that the invention was complete, or by describing distinguishing identifying characteristics sufficient to show that the applicant was in possession of the claimed invention" (Id. at 1104).

The Guidelines further state, "[f]or inventions in an unpredictable art, adequate written description of a genus which embraces widely variant species cannot be achieved by disclosing only one species within the genus" (Id. at 1106); accordingly, it follows that an adequate written description of a genus cannot be achieved in the absence of a disclosure of at least one species within the genus. *Bowie et al* (Science, 1990, 247:1306-1310) teach that an amino acid sequence encodes a message that determines the shape and function of a protein and that it is the ability of these proteins to fold into unique three-dimensional structures that allows them to function, carry out the instructions of the genome and form immunoepitopes. *Bowie et al.* further teach that the problem of predicting protein structure from sequence data and in turn utilizing predicted structural determinations to ascertain functional aspects of the protein is extremely complex. (column 1, page 1306). *Bowie et al* further teach that while it is known that many amino acid substitutions are possible in any given protein, the position within the protein's sequence where such amino acid substitutions can be made with a reasonable expectation of maintaining function are limited. Certain positions in the sequence are critical to the three dimensional structure/function relationship and these regions can tolerate only conservative substitutions or no substitutions (column 2, page 1306). Therefore, absent a detailed and particular description of a representative number, or at least a substantial number of the members of the genus of proteins, the

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skilled artisan could not immediately recognize or distinguish members of the claimed genus of proteins. Therefore, in accordance with the Guidelines, the description of proteins is not deemed representative of the genus proteins of I-M38 of the claim invention thus the claim does not meet the written description requirement.

### ***Conclusion***

#### ***Status of the Claims***

4. No claims are allowed.

Claims 1-7 are rejected.

5. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nina A. Archie whose telephone number is 571-272-9938. The examiner can normally be reached on Monday-Friday 8:30-5:00p.m. If attempts to reach the examiner by telephone are unsuccessful, the examiner supervisor, Shanon Foley can be reached on 571-272-0898. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR.

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Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/N. A. A./

Examiner, Art Unit 1645

Nina A Archie

Examiner

GAU 1645

REM 3B31

/Mark Navarro/

Primary Examiner, Art Unit 1645